JAK2 gene

Janus kinase 2

Normal Function

The *JAK2* gene provides instructions for making a protein that promotes the growth and division (proliferation) of cells. This protein is part of a signaling pathway called the JAK/STAT pathway, which transmits chemical signals from outside the cell to the cell's nucleus. The JAK2 protein is especially important for controlling the production of blood cells from hematopoietic stem cells. These stem cells are located within the bone marrow and have the potential to develop into red blood cells, white blood cells, and platelets.

Health Conditions Related to Genetic Changes

essential thrombocythemia

Some gene mutations are acquired during a person's lifetime and are present only in certain cells. These changes, which are called somatic mutations, are not inherited. Somatic mutations in the *JAK2* gene are associated with essential thrombocythemia, a disorder characterized by an increased number of platelets, the blood cells involved in normal blood clotting. The most common mutation (written as Val617Phe or V617F) replaces the protein building block (amino acid) valine with the amino acid phenylalanine at position 617 in the protein. This particular mutation is found in approximately half of people with essential thrombocythemia. A small number of affected individuals have a somatic mutation in another part of the *JAK2* gene known as exon 12.

The V617F *JAK2* gene mutation results in the production of a JAK2 protein that is constantly turned on (constitutively activated), which, in essential thrombocythemia, leads to the overproduction of abnormal blood cells called megakaryocytes. Because platelets are formed from megakaryocytes, the overproduction of megakaryocytes results in an increased number of platelets. Excess platelets can cause abnormal blood clotting (thrombosis), which leads to many signs and symptoms of essential thrombocythemia.

polycythemia vera

Somatic mutations in the *JAK2* gene are associated with polycythemia vera, a disorder characterized by uncontrolled blood cell production. The V617F mutation is found in approximately 96 percent of people with polycythemia vera. About 3 percent

of affected individuals have a somatic mutation in the exon 12 region of the *JAK2* gene.

JAK2 gene mutations result in the production of a constitutively activated JAK2 protein, which seems to improve the survival of the cell and increase production of blood cells. With so many extra cells in the bloodstream, abnormal blood clots are more likely to form. In addition, the thicker blood flows more slowly throughout the body, which prevents organs from receiving enough oxygen. Many of the signs and symptoms of polycythemia vera are related to a lack of oxygen in body tissues.

primary myelofibrosis

Somatic *JAK2* gene mutations are also associated with primary myelofibrosis, a condition in which bone marrow is replaced by scar tissue (fibrosis). The V617F mutation is found in approximately half of individuals with primary myelofibrosis. A small number of people with this condition have mutations in the exon 12 region of the gene. These *JAK2* gene mutations result in a constitutively active JAK2 protein, which leads to the overproduction of abnormal megakaryocytes. These megakaryocytes stimulate other cells to release collagen, a protein that normally provides structural support for the cells in the bone marrow but causes scar tissue formation in primary myelofibrosis. Because of the fibrosis, the bone marrow cannot produce enough normal blood cells, leading to the signs and symptoms of the condition.

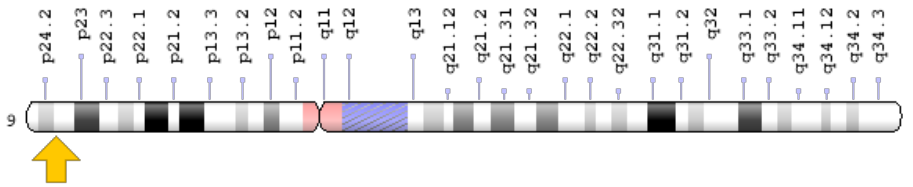
other disorders

Somatic *JAK2* gene mutations are also associated with several related conditions. The V617F mutation is occasionally found in people with cancer of blood-forming cells (leukemia) or other bone marrow disorders. Budd-Chiari syndrome, which results from a blocked vein in the liver, can also be associated with the V617F mutation when it is caused by an underlying bone marrow disorder. It is unknown how one particular mutation can be associated with several conditions.

Chromosomal Location

Cytogenetic Location: 9p24.1, which is the short (p) arm of chromosome 9 at position 24.1

Molecular Location: base pairs 4,985,086 to 5,128,183 on chromosome 9 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- JAK-2
- JAK2_HUMAN
- Janus kinase 2 (a protein tyrosine kinase)
- JTK10
- tyrosine-protein kinase JAK2

Additional Information & Resources

Educational Resources

- The Cell: A Molecular Approach (second edition, 2000): The JAK/STAT Pathway https://www.ncbi.nlm.nih.gov/books/NBK9870/#A2258

Scientific Articles on PubMed

- PubMed https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28JAK2%5BTI%5D%29+OR+%28Janus+kinase+2%5BTI%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- BUDD-CHIARI SYNDROME
  http://omim.org/entry/600880
- JANUS KINASE 2
  http://omim.org/entry/147796

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/JAKID98.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=JAK2%5Bgene%5D
- HGNC Gene Family: FERM domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/1293
- HGNC Gene Family: SH2 domain containing
  http://www.genenames.org/cgi-bin/genefamilies/set/741
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=6192
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3717
- UniProt
  http://www.uniprot.org/uniprot/O60674

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Reviewed: September 2014
Published: March 21, 2017

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